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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,711	05/08/2002	Audrey Goddard	P3230R1C001-168	8521

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KNOBBE, MARTENS, OLSON & BEAR, LLP
2040 MAIN STREET
IRVINE, CA 92614

EXAMINER	
KAUFMAN, CLAIRE M	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 11/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,711	GODDARD ET AL.	
	Examiner	Art Unit	
	Claire M. Kaufman	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-6,11-14 and 16-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-6,11-14 and 16-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 7/5/05, 9/15/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

The rejection of claims 14, 15, 21-25 under 35 USC 112, 2nd paragraph, is withdrawn in view of the Applicant's argument. By the definition of "about" in the specification [0012] cited by Applicant "at least about 20 nucleotides" must mean: At least the 20 nucleotides minus 10% of the 20. In this example, the claim would mean "at least 18 nucleotides in length". That is, "at least about X nucleotides" means: At least the length of the referenced (X) nucleic acid minus 10% of the referenced (X) nucleic acid sequence length.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 4-6, 11-14, 16-31 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention for the reasons set forth in the previous Office action

Applicant argues (p. 8) that the level of skill in the art was very high since the person of skill would generally have a Ph.D. with several years of experience. The argument has been fully considered, but is not persuasive. The skill in the art *generally* is high. However, the skill in the art as it relates to this tumor marker is not because it is not part of a well known family or does not share particular distinguishing features of structure or function that allow it to be assigned to a field in which a great deal is known. Even though the skill in the art of hybridization and sequence is very high, when one looks at the details of the instant invention including its use, the skill pertaining to that small area is not exceptionally high since so little was known about the claimed invention.

Applicant argues (p. 8 middle) that percent identity of a probe to its target is not usually common knowledge. The argument has been fully considered, but is not persuasive. The point

was meant to be that given a sequence one is trying to identify by probe, one would not routinely use a probe less identical than the given sequence, if at all possible. Having a probe less identical than the reference sequence invites cross-reactivity with sequences other than the reference sequence.

Applicant argues on p. 8, bottom, "...that the utility of the nucleic acid as a tumor marker for stomach and lung tumor is accepted...." Also, the specification teaches various methods of using the claimed nucleic acids, for example, in hybridization assays of samples and provides a working example of differential expression. The argument has been fully considered, but is not persuasive. For the reasons discussed in the previous Office action in the paragraph bridging pages 4-5, it is maintained that utility is not the same as enablement:

> [SEQ ID NO:77] does not encode a protein with a recognized/ characterized physiological/biochemical property. The non-identical nucleic acids (those which hybridize or are not 100% identical to SEQ ID NO:77 or its ORF) have not been shown to be underexpressed in any tumors or exists in nature. As to the state of the prior art, other nucleic acids usable for tumor markers had been identified, though none identified as such were identical or highly similar to SEQ ID NO:77. Therefore, the connection of SEQ ID NO:77 to tumors was not known. While the skill in the art for differential screening has existed for over a decade, interpretation of the results depends, for example, on relative or absolute levels of the difference(s), the ability to generalize to more than one cell culture or tumor type or, conversely, the ability to pinpoint a particular tumor type (*e.g.*, adenocarcinoma *versus* squamal), and repeatability of the differential expression both in terms of frequency/prevalence and quantity/sensitivity. Further, it was not routine to use as a tumor probe a nucleic acid less than 100% identical to the target nucleic acid. There are no working examples of nucleic acids at least 95% identical to or hybridizing under the recited conditions which are underexpressed in stomach or lung tumors other than SEQ ID NO:77 itself. The breadth of the claims is broad, encompassing structural variation and, in the case of claims 14, 16 and 19-31, no functional limitation. There is very little guidance or direction about using the claimed nucleic acid of SEQ ID NO:77 except the information that it is underexpressed in stomach and lung tumors. As discussed in previous Office actions, the specific type of tumor is not disclosed, nor are levels of expression, relative amounts or how many different tumor cDNA libraries from each tumor tissue were screened, for example. For all these reasons and those previous stated, it would require undue experimentation to use the invention as claimed.

As discussed, using the claimed nucleic acid as a hybridization probe to detect a different polynucleotide with an unknown function is not enabled. If the reference nucleic acid itself is

not enabled, then using it as a probe is not enabled. Just as an antibody is not enabled if it has no use of its own apart from binding a protein that is not enabled.

Applicant argues (p. 9, middle) that the need for further experimentation does not make it undue or preclude the invention from being enabled. The argument has been fully considered, but is not persuasive. Applicant is direct to the *Wands* analysis, for example, paragraph bridging pages 4-5 of the previous Office action discussing why it would require undue experimentation to use the claimed invention. As stated in *Brenner v. Manson* (*supra*), a patent "...is not a reward for the search, but compensation for its successful conclusion." It is maintained for the reasons of record that the instant invention is not at a point where specific benefit exists in a currently available form.

Applicant argues (paragraph bridging pages 9-10) that the Grimaldi Declaration describes assays conducted and explains results of Example 18, and when taken with the skill of the artisan and routine uses of nucleic acids such as for hybridization detection, it can be seen the instant invention is enabled. The argument has been fully considered, but is not persuasive. The Grimaldi Declaration was not dismissed, but fully assessed. It is maintained for the reasons set forth in the previous Office action and discussed above, that the nucleic acid is not enabled, for while it may show to some extent differential expression in stomach or lung tumors, the skilled artisan would not know how to use it in terms of enablement because as stated in the previous Office action, the literature cautions researchers from drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue. Without more specifics about necessary sample size, expression level range for normal and tumor tissues, how representative pooled samples are for individuals, the specification has not provided the invention in an enabled form. Other gaps in information include, for example, tumor type (etiology), and repeatability of the differential expression *both* in terms of frequency/prevalence and quantity/sensitivity.

Applicant argues (middle of p. 10) that even if a gene which is differentially expressed in tumors compared to normal tissue is not associated with a biological meaningful role in disease, it is nonetheless useful in diagnosis the existence of a tumor. The argument has been fully considered, but is not persuasive. It is maintained that differential expression does not enable diagnostic detection. The reasons for this have been set forth in the previous Office actions and

partially summarized in the immediately preceding paragraph. Diagnosis requires the expression be predictive of the presence of the tumor. It is maintained that it would require undue experimentation to use the polynucleotide for a diagnostic purpose because of reasons including necessary sample size to allow reasonable predictability of tumor presence, expression level range for normal and tumor tissues, how representative pooled samples are for individuals, tumor type (etiology) that would reasonably be expected to show repeatable detectable differential expression, and repeatability of the differential expression *both* in terms of frequency/prevalence and quantity/sensitivity. While the connection between differential expression and disease cause is not necessary, unlike the emphasis of Hu et al., the reliable or predictable connection between a particular nucleic acid's expression and presence of stomach or lung tumor is. As stated in the previous Office action on page 6:

> Applicants argue (p. 23) that the role of a gene in a cancer is not necessary to enable its use as a diagnostic tool for tumor detection. The argument has been fully considered, but is not persuasive. It is correct that the role of a gene need not be known, but the specification and/or prior art needs to enabled that particular gene to be used diagnostically. In this case, the prior art provides no information about the use of the gene and the specification does not provide an enabling disclosure for use of the PRO1357 nucleic acid as a diagnostic tool for stomach or lung tumors based on differential expression for the reasons discussed above and in previous Office actions. As to the claims drawn to nucleic acids not identical to SEQ ID NO:77 or its ORF, even if SEQ ID NO:77 were enabled for a diagnostic tool, nucleic acids not identical would not be because it was not routine or expected for the skilled artisan to use a probe not identical to the target nucleic acid sequence for detection of the target nucleic acid when the sequence of the target nucleic acid was known. Also, with unknown relative differences, it is unpredictable how different a polynucleotide probe could be from SEQ ID NO:77 and be used for differential expression.

Claims 4, 5 and 17-20 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons set forth in the previous Office action

Applicant argues (pages 11-12) that if there are sufficient identifying characteristics, *e.g.*, functional characteristic coupled to a structure, or hybridization conditions providing a limitation for claimed nucleic acids, and high skill in the art, that is sufficient for written description. In the instant application the function is higher expression in normal stomach or lung tissue compared to stomach or lung tumor tissue. The argument has been fully considered, but is not persuasive. The point is not the ability to hybridize. The point is that **neither** all hybridizing nucleic acids nor all nucleic acids 99% identical to SEQ ID NO:77 are included. Only those that naturally occur in stomach or lung are included. Applicant has disclosed no concept of which nucleic acid(s) which is not identical to SEQ ID NO:77 (or the coding region) are present in stomach or lung tissue. The specification does not convey to one of skill in the art, including recombinant DNA/protein technology, that the inventors were in possession of these non-identical naturally occurring nucleic acids. The specification does not provide information so the skilled artisan could readily envision such nucleic acids. For these reasons and those previously of record, the rejection is maintained.

Applicant argues (bottom of p. 12) that patents have been issued with claims to variant proteins and nucleic acids when such variants were never made. The argument has been fully considered, but is not persuasive. Each application is examined on its own merits.

Claim Rejections - 35 USC § 102

Claims 4-6, 11-14 and 16-31 remain are rejected under 35 U.S.C. 102(b) as being anticipated by WO 01/16318 or WO 00/12708 for the reasons set forth in the previous Office action.

Claims 14, 16, 21-25 remain rejected under 35 U.S.C. 102(b) as being anticipated by GenBank Accession BG529820 for the reasons set forth in the previous Office action.

Applicants argue that the instant application receives an effective filing date of 08/24/00 because the data of Example 18 was disclosed therein. The argument has been fully considered, but is not persuasive. Because the claims do not meet the requirements of 35 U.S.C. § 112, first

paragraph, as discussed above, and the earlier application likewise do not meet those requirements, the instant application does not receive benefit of priority to earlier filed applications. Even though SEQ ID NO:77 and 78 and the expression information of Table 18 were previously disclosed, enablement thereof has not been established as discussed above.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (571) 272-0873. Dr. Kaufman can generally be reached Monday, Tuesday, Thursday and Friday from 9:30AM to 2:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (571) 272-0829.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Official papers filed by fax should be directed to (571) 273-8300. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Claire M. Kaufman, Ph.D.

Patent Examiner, Art Unit 1646

November 10, 2005

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER